Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities

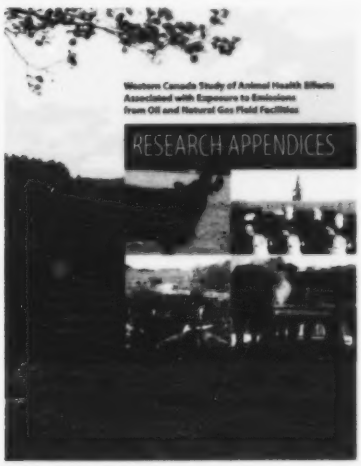
INTERPRETIVE OVERVIEW BY THE SCIENCE ADVISORY PANEL

A Study of 33,000 Cattle in British Columbia, Alberta and Saskatchewan

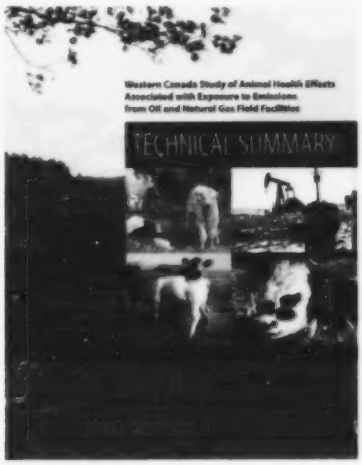
WISSA Western Interprovincial Scientific Studies Association

THE PUBLIC REPORT of the Western Interprovincial Scientific Studies Association (WISSA) presents the results of the Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities.

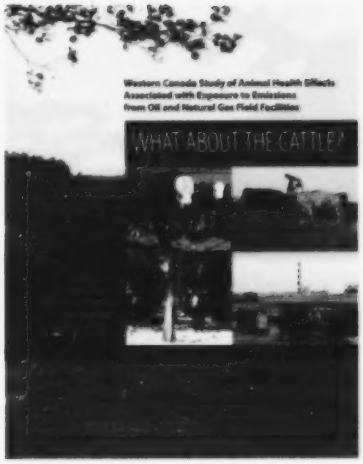
This is one of four publications that comprise the public report. The others are as follows:


Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities
RESEARCH APPENDICES

Research Appendices
A collection of 17 research appendices that presents the details of all research for the study


Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities
TECHNICAL SUMMARY

Technical Summary
A summary of the 17 research appendices that presents selected details of all research for the study


Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities
WHAT ABOUT THE CATTLE?

What About the Cattle?
Highlights of the study

106-07499

INTERPRETIVE OVERVIEW BY THE SCIENCE ADVISORY PANEL

Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities

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Introduction

This document summarizes the Science Advisory Panel's (SAP) interpretation of the findings of the *Western Canada Study of Animal Health Effects Associated with Exposure to Emissions from Oil and Natural Gas Field Facilities* (hereafter referred to as the WISSA study). The WISSA study is the largest and most comprehensive on-farm study of beef cattle health and production of this type ever undertaken in North America, in terms of both geographical scope and the number of farms and individual animals that were monitored.

The WISSA study was designed by the principal investigators and contractors in consultation with the SAP. The research protocols were implemented by the principal investigators and their research teams and research contractors. They reported regularly on their progress to the SAP. The SAP monitored ongoing adjustments to study design, implementation, analysis, interpretation, and communications, and reported to the Board of Directors of the Western Interprovincial Scientific Studies Association (WISSA) on a regular basis.

Historical context

This study arose as a result of concerns first expressed in the 1960s about the risk of health effects due to exposure to emissions from gas wells, plants, pumping stations, and other upstream petroleum facilities in Western Canada. The concerns were particularly centred on sour gas facilities, where there was the potential for exposure to hydrogen sulphide (H_2S). Studies in the early 1980s examined human health but did not resolve the concerns.

An important study by Mel Strosher, Alberta Research Council (Strosher, 2000), on emissions from flares, demonstrated that combustion in flares was often incomplete and that flares emitted a wide variety of chemicals. Since flares operate in many types of oil and gas facilities, this created additional concerns regarding the safety of flaring throughout the upstream petroleum industry, including both oil and natural gas sectors. These concerns were documented and focused in a series of multi-stakeholder workshops, symposia, and conferences held during the 1980s and 1990s on the issue. A central issue was the risk of health effects in cattle that might affect production. A literature review prepared for the Alberta Cattle Commission recommended studying the "possible toxicological effects on cattle from prolonged, low-level exposure to contaminants... with special attention to the reproductive and immunological systems" (Alberta Environmental Center, 1996).

In order to investigate the issue, several studies on cattle were undertaken in the 1990s, two of which were important predecessors to the WISSA study. While both studies had limitations, they provided important direction for the WISSA study. An Alberta-wide study using dispersion modeling of emissions to obtain estimates of exposure was conducted by Morgan Scott, University of Guelph (1998), using data collected in the 1980s, and was released in 1998. It demonstrated that there was no widespread problem associated with emissions from sour gas facilities, but could not rule out a limited local effect. The study by Scott had large statistical power but exposure to oil and gas emissions was modeled rather than directly measured and the health and productivity outcomes were limited to herd level outcome data extracted from the results of a mail survey. Scott (1998) recommended that "a more refined study is needed...future studies in this field must make use of valid on-farm exposure measurements and individual and herd-level health, productivity, and confounder data".

A second study based on detailed on-farm monitoring of individual animals over a several year period (1992 to 1996) was conducted by Cheryl Waldner, University of Saskatchewan (Waldner, 1999). Waldner's study used well-defined outcomes and accounted for many other known risk factors, but was limited by a smaller number of animals and by the technology of the exposure measurements that were available at the time. The study measured total sulphation and H_2S deposition as exposures and the proximity of individual pastures to various facility types were determined. The study also estimated flaring exposure for each herd using flaring volumes reported in the study region to the

Alberta Energy Utilities Board (AEUB). Models were developed to look for associations between various health outcomes in the study cattle and these exposures. Most of the models that examined total sulphation and H_2S exposures over the 3-year period showed no association with animal health outcomes. However, there was at least one time period where exposure to either total sulphation or H_2S deposition was associated with an increase in the risk of either nonpregnancy, abortion, stillbirth, or prolonged calving interval. Furthermore, in 3 of 4 years, increased cumulative exposure to sour flare volumes during gestation was associated with an increased risk of stillbirth.

Waldner (1999) expressed concern about the limitations of the exposure measurements. Although the measurements were considerably better than the very high uncertainty that had been suggested for dispersion model estimates, there were still questions about the reliability and validity of some exposure data, especially for the H_2S deposition measurements. The completeness of reported flaring volumes and the relationship between the exact location of flaring and specific cattle locations was difficult to verify. As a result, Waldner (1999) stated that her study, "together with previous studies, suggests the need to explore the association between emissions from sour gas processing facilities and reproductive parameters in *cattle with more refined techniques for exposure analysis*".

The current WISSA study addressed many of the primary questions at the centre of the unresolved controversy. The WISSA study used better measures of exposure to specific emissions, and with a sufficient number of herds and animals to give the necessary statistical power, to determine if exposure to these emissions influenced animal health or reproductive performance.

Study design

The WISSA study was designed to meet two essential goals: 1) to determine if chronic exposure to emissions from the oil and gas industry influences the health and reproductive performance of cattle and wildlife (starlings) in Western Canada, and 2) to provide useful information for cow-calf producers on factors affecting herd productivity. This overview will focus predominantly on the first of these goals.

The design required that locations of individual cows in all participating beef herds from Alberta, Saskatchewan, and northeastern British Columbia be monitored closely wherever they were pastured or penned in order to accurately and precisely determine their exposure status. The resulting air-monitoring program also created the opportunity to study possible effects of emissions exposure on a representative wildlife species, the European Starling, that shared the same environment as the cattle.

The WISSA study collected accurate data on animal health outcomes in subject herds and on the concentrations of specific contaminant emissions in their environment. Data on other known risk factors affecting animal health were also examined. These included risk factors such as the cow's age and breed, whether the cow was born on the farm or purchased, the cow's body condition score, and various herd management practices. The number of animals and data points in the research protocol that governed the WISSA study were designed to be large enough to provide the statistical power (i.e., ability to detect significant associations if they existed) necessary to test the hypotheses of primary interest.

The primary hypotheses governing the study design involved the assessment of possible adverse impacts of emissions on reproduction and herd productivity. Secondary hypotheses were examined using the unique opportunities presented to assess lesions in the respiratory, immune, and nervous systems of aborted, stillborn, and live-born calves that died, and their possible association with emissions. The WISSA study also capitalized on the opportunity to assess results that emerged from research team's observations made from the data collected.

Exposures

The WISSA study measured concentrations of many airborne contaminants. The contaminants considered to be most important and representative of a class of important compounds were selected for detailed analysis.

The exposures measured and assessed were:

(1) sulphur dioxide (SO_2,)
(2) hydrogen sulphide (H_2S)
(3) volatile organic compounds (VOCs) measured as benzene
(4) VOCs measured as toluene

Passive air monitors were used to monitor the concentrations of SO_2, H_2S, and VOCs measured as benzene and toluene. These monitors were located on or near all occupied pastures and wintering areas for each herd during the course of the study. From April 1, 2001 to January 2003, concentrations of SO_2 and VOCs were measured more than 9,800 times at 1,200 sites, and H_2S was measured more than 6,300 times at 1,100 sites. This represents the largest compilation of measurements on these parameters of air quality in rural Western Canada to date and is a valuable contribution to the understanding and knowledge of air quality in the region. Highlights of these data are summarized in the table below.

Summary of monthly measured air concentrations at each sampling site for 2001 and 2002

Source: Research Appendix 3.

Air monitoring outcomes (concentrations)	Arithmetic mean	5th percentile	Median	95th percentile	Geometric standard deviation
SO_2 (ppb)	0.65	0.16	0.52	1.62	2.2
H_2S (ppb)	0.20	0.05	0.14	0.53	2.4
Benzene (ng/m^3)	290	0	220	740	4.9
Toluene (ng/m^3)	440	34	240	970	3.9

During this same time period, information on the locations of over 39,000 animals from 205 herds on 3,355 different parcels of land was recorded for each half-month interval, resulting in the documentation of almost 3.8 million animal locations. This information was used to assign to each animal in the study an average value for each of the measured exposures for each month of the study. Well-site density was also examined as a secondary exposure measure. Each animal's monthly exposure was then averaged to create appropriate cumulative exposure values for biologically relevant risk periods for each outcome. This process represented a truly remarkable achievement by the researchers in establishing, as closely as possible, individual cow exposures.

Summary of individual animal monthly exposures calculated on the basis of the air concentration data at a given location for the time the animal spent at the location

Source: Research Appendix 5

Air monitoring outcomes (exposures)	Arithmetic mean	5th percentile	Median	95th percentile	Geometric standard deviation
SO_2 (ppb)	0.7	0.2	0.5	1.7	2.2
H_2S (ppb)	0.19	0.05	0.14	0.51	2.3
VOCs measured as benzene (ng/m3)	314	27	244	780	2.5
VOCs measured as toluene (ng/m3)	422	33	236	992	2.7

Exposures to fine particulate matter ($PM_{1.0}$) and polycyclic aromatic hydrocarbons (PAHs) were measured a total of 365 times near the calving area for 32 herds. Data collected in a subset of 22 of these herds was used to study potential effects of PM and PAH exposure on immune function. Highlights of the monthly average $PM_{1.0}$ data follow.

Summary of monthly measured air concentrations at each sampling site for 2001 and 2002

Source: Research Appendix 3.

Air monitoring outcomes (concentrations)	Arithmetic mean	5th percentile	Median	95th percentile	Geometric standard deviation
$PM_{1.0}$ ($\mu g/m^3$)	8.7	2.9	7.5	21.7	1.8

Compared to other similar data collected in rural areas in Western Canada, this study was successful in capturing a relatively wide range of all the selected air contaminants, which was essential for the power of the study and

which greatly aided interpretation of the findings. As expected, the concentration of air contaminants generally correlated with the density of local oil and gas activity and there were very few examples of unexpectedly or exceptionally high levels of any contaminant observed. In general, concentrations of air contaminants tended to be seasonal and highest in wintertime. The WISSA study demonstrated that the use of passive monitor technology, such as the SO_2 sampling devices that are commercially available,[1] is feasible in a large field study in rural areas. This study also successfully employed a solar powered active PM monitor adapted specifically for remote field deployment in this study[2].

Health outcomes

The five primary health outcomes studied in the beef cattle study were the following:

(1) Nonpregnancy
(2) Length of breeding-to-calving interval (BCI)
(3) Abortion
(4) Stillbirth
(5) Calf mortality

Nonpregnancy represented the risk that the cow would not conceive or become pregnant. The BCI was used as an estimate of how long it took the cow to become pregnant. Abortions were defined as either an observed premature calving, judged to be at least 1 month before full term, or an assumed calf loss when a cow was diagnosed as pregnant but failed to calve. Stillbirths were defined as any full-term calf that was born dead or died within 1 hour of birth. Calf mortality included any calf that died from 1 hour after birth up to 3 months of age.

In addition, several secondary health outcomes were measured using nested projects within the larger study. These included the pathology and/or function of body systems that in the past had been suspected of being adversely affected by emissions. There were four secondary measures in the cattle study that included the risk of treatment of calves, respiratory pathology in calves, neuropathology in calves, and immune system pathology and function in calves and yearling cattle. Immune system pathology was examined by looking for lesions in calves that died during the study. Immune system function was assessed in two ways: first, by measuring the antibody response to the administration of a rabies vaccine in a subgroup of yearling cattle in 27 study herds, and second, by counting white blood cell types (B-lymphocytes and four T-lymphocyte subtypes) in blood samples taken from the same subgroup of yearling cattle and also neonatal calves from a larger subset of study herds.

Outcomes measured in starlings were reproductive success and immune system structure and function. Starling reproductive success outcomes included hatching success, fledging success, tarsal bone length, and first primary feather length. Immune system structure outcomes included size of the spleen and the bursa of Fabricius relative to total body size and the relative numbers of two types of white blood cells. Immune system function outcomes included several measures of antibody production and T-lymphocyte response.

The findings related to herd productivity in the beef cattle study were based on the assessment of individual animal data rather than the herd-level survey approach used in most previous studies. There are few benchmarks against which to compare results, given the differences in the ways in which the data were collected in the WISSA study. What few data that do exist from other studies, however, suggest that the overall experience of cow-calf producers in Western Canada was similar to that in other comparable regions of North America. For example, the average 90-day mortality rate of 3.6% for calves was consistent with earlier studies, either much smaller studies or those where data were collected using questionnaires. This consistency reinforces confidence that the more detailed findings in the WISSA study can be generalized to the beef industry at large.

The WISSA study yielded a wealth of data that can be used to benchmark productivity indices in the future. Some highlights are summarized in the chart on the following page.

[1] Maxxam Analytics Inc., Edmonton AB. [2] AirZOne One, Mississauga, ON.

Productivity benchmarks	5th percentile	25th percentile	50th percentile	75th percentile	95th percentile
% of cows in each herd that were not pregnant 2001	2.0%	4.2%	6.3%	8.5%	13.0%
% of cows in each herd that were not pregnant 2002	2.1%	5.1%	7.2%	10.0%	16.9%
% of cows in each herd that aborted 2001 to 2002	0.0%	0.6%	1.3%	2.4%	4.0%
% of calves in each herd that were stillborn 2002	0.0%	1.3%	2.5%	3.9%	6.4%
% of calves in each herd that died before 3 months of age 2002	0.0%	1.6%	2.9%	5.1%	8.2%
% of calves that were treated for any reason	0.0%	1.8%	6.5%	13.6%	48.1%

Analyses

The WISSA study first examined whether there were any associations between the exposure measures and the primary health outcomes in beef cattle. This analysis was performed using statistical modeling procedures that corrected for the effects of confounding risk factors, such as cow age and breed, and weather factors, in addition to accounting for the similarity of cows within a herd. The first analysis examined whether increased exposure was associated with a change in the risk of nonpregnancy. The next examined whether the same exposure was associated with a change in the risk of abortion, and so on through the remaining possible pairings of exposures and outcomes. Some outcomes had more than one exposure period examined. The WISSA study also examined whether there were any associations between the exposures and secondary outcomes measures over their relevant exposure periods.

Hypotheses were classified as primary or secondary for several reasons. Because a study only can be designed to reliably test a few key hypotheses, the principal questions must be carefully prioritized. From a purely statistical perspective, the more associations one looks for, the more likely spurious associations are to appear. These spurious associations are ones that are due to chance. The WISSA study was specifically designed to investigate whether there were associations between the four exposures and the five primary outcomes in beef cattle. The primary outcome measures represented key clinical reproductive and calf mortality outcomes in the cattle.

Secondary hypotheses were classified as such because the study was not designed to explicitly address them. They involved either outcomes (e.g., treatment) that were not as precisely measured as the primary outcomes (e.g., mortality), outcomes where the sample size could not be controlled by the researchers (e.g., pathology), or exposures and outcomes that could only be measured in a subset of the herds in the WISSA study (e.g., immunology). As such, it is more difficult to interpret associations identified as a result of tests of secondary hypotheses. This was especially true with secondary outcomes like immune function, which involved numerous comparisons of counts of multiple cell types.

The hypotheses can be summarized as questions shown in the following table.

Study questions
In beef cattle : *Were exposures to emissions from oil and gas facilities associated with an increased frequency of:* PRIMARY OUTCOMES a) non-pregnancy, abortion, or stillbirth? b) lengthening of the interval from first bull contact to calving? c) calf mortality? SECONDARY OUTCOMES d) treatment of calves with pharmaceuticals? e) lesions in tissues of the respiratory tract? f) lesions in tissue of the nervous system? g) lesions and/or functional impairment of the immune system? EMERGENT OUTCOMES h) histopathological lesions in muscle and thyroid tissues from aborted, stillborn, and postnatal calf deaths?
In wild starlings: *Were exposures to emissions from oil and gas facilities associated with:* i) impaired reproductive success or development? j) lesions and/or functional impairment in the immune system?

Beef study findings

Primary outcomes and hypotheses

General

Most of the hypotheses tested showed no association between exposure and health outcome. There were no associations between the measured exposures (SO_2, H_2S, and VOCs measured as benzene or toluene) and the risk of nonpregnancy, abortion, or stillbirth. This was a particularly important finding, given the historical concerns by some that these exposures might be associated with reproductive problems in beef cattle. The findings of the WISSA study clearly indicated otherwise across the measured range of exposures. Similarly, increased exposures to SO_2, H_2S, and VOCs measured as toluene showed no associations with breeding-to-calving interval (BCI), and increased exposures to H_2S, and VOCs measured as benzene or toluene showed no associations with changes in calf mortality. Only a few of the hypotheses tested suggested an association between exposure and primary health outcomes. The highest measured exposures to VOCs measured as benzene were associated with an average 3-day increase in time to calving, and the highest measured exposures to SO_2, either throughout gestation or during the last trimester, were associated with a relative 1.4-fold increase in the risk of calf mortality.

Nonpregnancy, abortion, and stillbirth

There were no associations between any of the primary exposures and the risk of nonpregnancy, abortion, or stillbirth across the measured range of exposures. This finding differed from the previous study by Waldner (1999) that found in 5 of 18 models that there was an association between total sulphation or H_2S deposition and a measure of reproductive success. Furthermore, Waldner found in 3 of 4 years studied that the risk of stillbirth was associated with increasing cumulative exposure to estimated flaring volumes. Scott (1998) found no associations with nonpregnancy, and even suggested a decreased risk of stillbirth in both beef and dairy herds was associated with increasing sour gas processing emissions.

Several factors are likely responsible for these differences, including improvements in exposure measurement technology, changes in the level of exposures in the study area, and differences in the measurement of the stillbirth outcome. Waldner had expressed concern about the relatively unrefined techniques for exposure analysis used to test associations in previous studies. The passive monitors used in the WISSA study were superior to the measures of facility proximity, flaring volume estimates, and dry deposition technology used in the previous Waldner study, and the models of exposure reported in the Scott study.

The maximum exposures of the cattle to emissions associated with flaring were very likely higher in the earlier studies. The AEUB reported substantial reductions in both solution gas flaring and venting during the period between these studies. These changes followed the AEUB adoption of the Clean Air Strategic Alliance (CASA) Solution Gas Management Framework for flare reduction. The finding of no effects on these reproductive parameters in the WISSA study could reflect the lower range of exposures that resulted from the adoption of the CASA framework for both flare and venting reduction. The much greater size of the present study gave it greater ability to detect smaller differences. If there was an association at these lower exposures, we would have expected to see it. This is supported by the WISSA study's ability to find a relatively small difference (1.8%) in calf mortality. It seems unlikely, therefore, that the present study "missed" an association between the primary exposures and stillbirth risk.

The definition of stillbirth *per se* was not the same in the Waldner (1999) and WISSA studies. The earlier Waldner (1999) study defined a stillbirth as a calf that was born dead or died within the first *twenty-four hours of birth.* The WISSA study defined stillbirth as born dead or died *within one hour of birth.* Calves that died in the WISSA study from 1 to 24 hours of birth were classified as calf mortalities instead of stillbirths, which is a more accurate description of their outcome. More than 22% of calf mortality in the WISSA study occurred between 1-24 hours of age, thus, these mortalities would have been defined

as stillbirths in the previous Waldner study. It is possible, therefore, that the associations of exposure with stillbirth seen in the previous Waldner study would have become associations with calf mortality had the same case definitions for stillbirth and calf mortality been used.

Length of the interval between calvings

Increased exposures to SO_2, H_2S, and VOCs measured as toluene during the 30-day period after the bull was first turned out with the cows showed no associations with BCI. Exposure during the same time period to VOCs measured as benzene was associated with a relatively small increase in the interval from breeding to calving. Cows exposed to the highest 25% of VOCs measured as benzene had a 3-day increase in the BCI compared to cows in the lowest 25% of measured exposures. The practical or biological significance of the average 3-day delay in a BCI that averaged 305 days (SD = 23 days) is unknown.

The goal of examining the BCI is to estimate any potential effect of exposure on the time necessary for the cow to conceive. However, there will always be some error in the estimate in time to conception because the BCI is composed of two elements (the time to conception and the gestation period), each of which may vary. The time to conception is uncertain because there is no practical way (in large commercial herds) to determine how quickly a cow becomes pregnant after the bull is introduced into the herd. The gestation period can vary substantially across breeds and the ability to completely account for these differences was limited given the variety of breeds used and complexity of cross-breeding programs. An average difference of 3 days is small compared to the differences in gestation periods across breeds and for individual animals within breeds.

Calf mortality

Increased exposures to H_2S and VOCs measured as benzene or toluene showed no associations with changes in calf mortality. Increased exposure to SO_2 throughout gestation and during the last trimester was associated with a small increase, in absolute terms, in the risk of calf death. Calves exposed to the highest measured concentrations of SO_2 were about 1.4 times more likely to die than calves exposed to the lowest measured concentrations. For example, for an average bull calf born to a heifer, the risk of dying would be increased by 1.8% in the most exposed calf as compared to the least exposed calf.

Because the relative increase between lowest and highest exposure levels in the risk of calf mortality was less than two (a rule of thumb for making causal inferences), the association was considered relatively weak. Where the relative risk is small, as it was here, there is the potential that uncontrolled confounding could influence the finding despite the large number of other risk factors accounted for in this analysis.

The associations with calf mortality were seen at levels of SO_2 far below those causing significant biological effects, death, or disease in other studies in the literature. The association between exposure and calf mortality was not inconsistent with biological theory, but current knowledge of the toxicology of SO_2, which is among the most extensively studied individual air pollutants, would not have predicted such a result at these low levels of exposure. However, the potential effects of SO_2, H_2S, and VOCs were not being studied in isolation. These compounds were selected as surrogates for the complex mixture of contaminants released during operations by upstream oil and gas facilities. The highest concentrations for each of these surrogates were associated with different types of industry operations and the highest concentrations of each compound were found at slightly different locations throughout the study area. These data show that calves born to cows from areas with the highest concentrations of SO_2 were most at risk. It is possible that other air contaminants or mixtures of contaminants that occurred in association with SO_2, might have been responsible for this finding.

Given the consistency of findings within this study (in exposure periods and analytic approaches), and notwithstanding the low exposure levels, and the relatively small size of the effect, the association steadily increased with exposure and is biologically plausible. Taken together,

these findings could reflect a direct effect of SO_2 exposure on mortality, or the effects of a SO_2-related contaminant, or mixture of contaminants on calf mortality.

Secondary outcomes and hypotheses

General

Most of the secondary hypotheses tested in the beef study showed no association between exposure and health outcome. There were no associations between any of the exposures and neuropathology in calves. There were no associations between SO_2 or H_2S and immune system pathology and function in calves and yearling cattle, nor were there any associations between postnatal exposure to SO_2 or H_2S and respiratory pathology in calves. Cattle treatment risk was associated with all four primary exposures; however, a proper "dose effect" was only seen with increasing exposure to H_2S. Exposures to VOCs measured as benzene and toluene were associated with a small increase in the occurrence of lung pathology in calves that died after 3 weeks of age.

Well site density was not associated with any of the outcome measures. In addition, there were no associations between airborne concentrations of $PM_{1.0}$ or PAHs and white blood cell (lymphocyte) counts, or antibody response to a rabies vaccine.

Treatment of calves with pharmaceuticals

In the context of this study, "treatment" means that the producer reported that the calf was given a pharmaceutical product for the treatment of an observed illness or, less frequently, to prevent a perceived disease threat. Calves that survived to one month of age and that were exposed to higher levels of some emissions in the first month of life were more likely to receive treatment before turn-out onto summer pasture. The nature and purpose of the treatment was not recorded in detail for most herds and treatment choices varied considerably from one producer to another. Calf treatment risk was associated with all four exposures; however, a systematic "dose-effect" pattern consistent with a causal effect was only seen with increasing exposure to H_2S. This was the only association between H_2S exposure and a health outcome identified in this study. This effect was not observed in an alternate analysis which examined the risk (probability) of treatment for all calves associated with exposure during the first month of life.

Given similar findings of associations between exposure and increased calf mortality, the risk of respiratory lesions, and changes to the immune system, these findings cannot be dismissed. However, considering the lack of consistency across models and a clear exposure-response relationship, the biological significance of the association between exposure and treatment risk appears to be limited.

Respiratory system

Exposures to SO_2 and H_2S were not associated with more frequent occurrence of lesions in the respiratory system in calves examined *post mortem*. Exposures to VOCs measured as benzene and toluene were associated with a small increase in the occurrence of lung pathology in calves that died after 3 weeks of age. It is unlikely that this finding could be completely explained as the result of the direct irritant effects of inhalation on lung tissue. Based on current knowledge, the chemicals included among VOCs (including benzene and toluene) would not be expected to produce substantial direct effects to the epithelium of the respiratory tract at these relatively low levels. Nevertheless, there could have been an effect of other airborne contaminants that are reflected in VOCs measurements. It is also possible that the small increase in the incidence of lung pathology was secondary to mildly compromised immune function related to VOC exposures. The most common lung lesions in this age group of calves were consistent with the effects of infectious causes of pneumonia. Immuno-compromised calves may have been more likely to develop pathological changes in the lung.

Nervous system

Exposure to emissions from oil and gas facilities was not associated with an increase in the occurrence of lesions in the nervous system in beef calves.

Immune system

Increasing exposure was not associated with pathological changes to immune system tissues. Also increasing exposure was not associated with changes in antibody response to vaccination in the yearlings examined in 27 herds or in most selected white blood cell counts in either the yearlings or a relatively small group of calves (325 in total) where these parameters were measured. There were a few instances where exposures to VOCs were associated with decreases in the counts of a few specific white blood cell types associated with immunity. *In utero* exposure to VOCs measured as benzene was associated with a decrease in numbers of two specific types of white blood cells (CD4 and CD8 T-lymphocytes) in calves. Reduction in production of some white cells is a known effect of benzene but similar findings have not been reported at such low levels. In calves, a similar association was seen between exposure to VOC measured as toluene and CD4 T-lymphocyte cell counts. In yearling cattle, increasing exposure to VOCs measured as toluene but not as benzene was also associated with a decrease in the number of CD4 T-lymphocyte white blood cells.

As noted earlier, the appearance of the lesions in the respiratory system suggests that there may have been subtle changes in the immune system of the animals. However, decreased cell counts were not associated with a concomitant increase in either mortality or history of treatment in the relatively small group of neonatal calves where lymphocyte counts were measured. Unfortunately, the size of this group was too small to provide sufficient statistical power to account for known confounding factors identified in the analysis of treatment risk, such as cow age and the month the calf was born. The resulting power to assess whether decreasing cell counts actually affected treatment risk was therefore very limited. As a result, the significance of these observations remains uncertain.

Emergent outcomes and hypotheses

This part of the study tested hypotheses that emerged from outcomes that were identified from an analysis of unexpected patterns in the diagnostic pathology data and particularly observations that dealt with a histopathological study of muscle and thyroid tissues from aborted, stillborn, and postnatal calf deaths.

Muscle and thyroid tissues

Increased *in utero* exposure to SO_2 was associated with a small increased risk of myopathy (muscle pathology) in beef calves. Increased *in utero* exposure to VOCs measured as benzene was associated with a small increased risk of thyroid gland lesions in beef calves. Because there is no immediate explanation for these findings, further investigation may be warranted. Since the lesions in the muscles were similar, although not identical, to lesions associated with various vitamin and trace mineral deficiencies, the potential role of nutritional risk factors is the subject of ongoing analysis.

European starling study findings

Secondary outcomes and hypotheses

Starlings were selected for study of emission effects because they nest widely throughout the region and have been previously studied as sentinels for environmental problems. Findings for this aspect of the study were secondary outcomes in that they were constrained by the study design for making exposure observations in beef cattle.

Reproductive success and development

None of the exposures were associated with the hatching or fledging success in European starlings. Exposure was also not generally associated with nestling growth. However, exposures to VOCs measured as benzene and toluene were associated with a small decrease (7-8% respectively) in bone growth (measured as tibio-tarsal length) in nestlings exposed to the highest quartile of concentrations, compared to the lowest quartile. Feather growth was not affected. The small decrease in bone growth did not affect the young birds' ability to fledge successfully and the significance of this on the future health and survival of the bird is unknown.

Immune system pathology and function

None of the exposures were associated with changes in the primary measures of the immune system in starlings, namely antibody production and T-lymphocyte response to a mitogen (PHA) as an indicator of cell-mediated immune response, nor were any exposures associated with any somatic measures of the immune system such as organ/body weight ratios or microscopic structure.

Increased exposures to SO_2 and H_2S were associated with increased heterophil/lymphocyte ratios in one year of the study. This likely had little effect on nestling immune competence.

Summary assessment

The primary objective of the WISSA study was to determine if chronic exposure to emissions from activity of the oil and gas industry influence the health and reproductive performance of cattle in Western Canada. A previous study by Waldner (1999) and anecdotal observations indicated that this issue merited making it the primary area of investigation. The nature of the present study also offered the opportunity of collecting useful information for cow-calf producers on factors that affect herd productivity and, in a much smaller parallel study, to collect information on the health of wild starlings that shared the same environments as cattle.

Looking at the results from a broader perspective, across all of the exposures and outcomes in the two studies, the most predominant pattern one sees is that there were no associations between the measured exposures and most of the health outcomes. Looking more specifically at the primary reproductive outcomes in beef cattle, no associations were found among any of the exposure measures and the risk of non-pregnancy, abortion, or stillbirth. The consistency of these findings across all exposures and the primary reproductive outcomes strongly suggests that cows exposed to the higher concentrations of SO_2, H_2S, or VOCs measured as benzene and toluene, within the ranges documented across Western Canada during the study period, were not at increased risk of nonpregnancy, abortion, or stillbirth. Also, the sulphur-containing exposures (SO_2 and H_2S) showed no associations with secondary outcome measures in the respiratory, immune, and nervous systems.

Where effects were found, some were small and, while statistically significant, may be of limited biological relevance or practical importance. The most important exception would appear to be the association found between exposure to SO_2 and the increased risk of calf mortality. The absolute increase in the risk of mortality was 1 to 2% above background at the highest measured levels of exposure.

There was also a small increase in the risk of calves receiving treatment after 1 month of age with increasing postnatal (first month) exposure to H_2S. The findings of associations between at least one of the sulphur-containing exposures (SO_2 and H_2S) and both calf mortality and calf treatment adds credence to the suggestion that these associations were real and representative of a true biological effect within the study subjects. Also, the finding that there was a greater risk of lesions in the calf skeletal or cardiac muscle with increasing prenatal exposure to SO_2 might suggest that skeletal or cardiac myopathies could have influenced the level of calf mortality. The outcomes associated with SO_2 itself may reflect a true effect of SO_2 exposure, or an air contaminant or mixture of contaminants closely associated with SO_2 (i.e. SO_2 acted as a surrogate).

The only outcome associated with H_2S was a relatively weak one with increased risk of treatment.

Increased exposure to VOCs measured as benzene was associated with a few seemingly disparate outcomes that had little or no measurable effect on calf survival. These associations were a small increase in the BCI in cows, a greater risk of calf respiratory lesions (postnatal exposure) and thyroid lesions (pre- and postnatal exposure), a lower count of CD4 and CD8 T-lymphocytes in calves, and a slightly shortened tarsal bone in nestling starlings. There appears to be no common biological principle that would tie these all of these associations together, although the effects on the calf respiratory system and lower CD4 and CD8 T-lymphocyte

cell counts could reflect slight immuno-compromise in these animals.

Looking across the results related to the four selected exposures shows that there were three quite distinct types of exposure. SO_2, H_2S, and VOCs did not correlate equally well with proximity to or reported emissions from all types of upstream oil and gas facilities. Results from VOCs measured as toluene were similar to those found for VOCs measured as benzene and did not add much information to the picture gained from VOCs measured as benzene. However, examination of the remaining three primary exposures, SO_2, H_2S, and VOCs measured as benzene showed that only once, with calf treatment, did all three exposures show an association with a specific outcome. All other associations tended to link one exposure type to one outcome. Further, measures of well site density usually did not correlate well with the measured primary exposures, and there were no associations between well site density and any of the health outcomes in the study. Taken together, these observations provide support for the greater sensitivity and specificity of the measures of SO_2, H_2S, and VOCs used in this study compared to proximity to facility measures used in this or previous studies.

Despite the application of very conservative statistical techniques to control the potential for false positive associations, some of these findings may have occurred by chance alone, while others could point the way to new knowledge and deserve close scrutiny by the scientific community. There were also some findings that should be interpreted carefully considering the uncertainties in outcome measurements, such as the finding of a 3-day difference in the BCI in those herds with a higher exposure, and the finding of more frequent treatment of calves after the first month of life in calves with higher exposures during the first month of life.

Because the conclusions for this type of study are based on inferences about population averages, the findings cannot be used to make predictions about individual animals or herds. The descriptive statistics are valid only for application to populations; individual findings at the herd level can and do vary widely.

The WISSA study has been a massive and challenging undertaking, directed by an innovative management model, conducted using advanced scientific methods and overseen by a group of scientific peers. Those working in a number of fields including air-quality monitoring, cattle health and production, and wildlife toxicology will use the baseline information collected. The study was also an important example of the use of both domestic animals and wildlife species as sentinels for the impact of industrial emissions on the environment.

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